Remarks

Amendments to the Claims

Claim 21 is amended to recite "a cell in which a chimeric protein has been bound to the surface of the cell, wherein each chimeric protein comprises an MHC molecule and an immunoglobulin chain, wherein the immunoglobulin chain is a heavy chain comprising a variable region which is C-terminal to the MHC molecule; wherein the chimeric protein associates to form molecular complexes comprising at least two chimeric proteins per complex." This amendment is literally supported in the present specification and in Serial No. 60/058,573, as discussed below in connection with the rejection under 35 U.S.C. § 112 ¶ 1 (new matter).

Claim 21 also is amended to recite that the immunoglobulin chain is a heavy chain and "comprises a variable region which is C-terminal to the MHC molecule." This amendment merely incorporates subject matter recited in dependent claim 53 and clarifies the relative locations of the immunoglobulin heavy chain variable region and the MHC molecule. See the discussion below in connection with the rejection under 35 U.S.C. § 112 ¶ 1 (new matter).

Claims 53 and 56 are amended to recite that the immunoglobulin heavy chain is not an IgG_1 heavy chain. This amendment is literally supported in the present specification (page 3, line 22) and in Serial No. 60/058,573 (page 4, lines 10-11).

Applicants respectfully request entry of the amendments. The amendments add no new matter and do not require a new search. They also present the claims in better form for appeal.

The Objection to the Amendment Filed April 5, 2004

The Final Office Action contends that the preliminary amendment filed April 5, 2004 "added material which is not supported by the original disclosure." Final Office Action at page

2. The April 5, 2004 amendment did not add new matter. The present application is a division of Serial No. 09/789,720 which, in turn, is a division of Serial No. 09/150,622. Applicants incorporated the parent applications' disclosures into the present application in case any portion of the present specification was lost or inadvertently omitted when the application was filed. The disclosures of the three applications are identical. The incorporation by reference did not introduce any new matter into the present application's disclosure. To advance prosecution, however, the specification is amended to delete the incorporation by reference of Serial Nos. 09/789,720 and 09/150,622.

Applicants respectfully request entry of the amendment. The amendment complies with a requirement set forth in the Final Office Action. It does not add new matter and does not require a new search of the claims.

Clarification of the Brief Description of Figure 1B

As requested, the brief description of Figure 1B is amended to clarify the identity of the nucleotide and amino acid sequences shown in the figure. Applicants respectfully request entry of the amendment, which is supported by Example 9 of the specification. The amendment complies with a requirement set forth in the Final Office Action. It does not add new matter and does not require a new search of the claims.

Rejection Under 35 U.S.C. § 112 ¶ 1

The Final Office Action asserts that claims 21-23 and 53-56 contain new matter. Final Office Action at pages 2-3. The Final Office Action also contends the pending claims are

entitled only to the April 5, 2004 filing date of the present application. Final Office Action at page 3. Applicants respectfully traverse the rejection and request its withdrawal.

A specification must convey clearly to those skilled in the art that the applicant invented the claimed subject matter. *In re Ruschig*, 379 F.2d 990, 996, 154 U.S.P.Q. 118, 123 (C.C.P.A. 1967). The subject matter recited in claim 21 as amended is disclosed in the present specification and is entitled to the September 11, 1997 filing date of priority application Serial No. 60/058,573. The table below compares the recitations of independent claim 21 as amended and disclosure in the present specification and in the '573 priority specification:

recitation of claim 21	**present specification**	**Serial No. 60/058,573**
a cell in which a chimeric protein has been bound to the surface of the cell	a cell in which a chimeric protein has been bound to the surface of the cell *page 3, line 29 to page 4, line 1*	a cell in which a chimeric protein has been bound to the surface of the cell *page 4, lines 16-17*
each chimeric protein comprises an MHC molecule and an immunoglobulin chain	the chimeric protein comprises an MHC molecule and an immunoglobulin chain *page 4, lines 1-2*	the chimeric protein comprises an MHC molecule and an immunoglobulin chain *page 4, lines 17-18*
the immunoglobulin chain is a heavy chain comprising a variable region which is C-terminal to the MHC molecule	Figure 1A, which shows an immunoglobulin heavy chain comprising a variable region fused C-terminal to an MHC molecule . . . a fusion protein of the invention in which an immunoglobulin heavy chain is C-terminal to an MHC molecule. *page 13, lines 9-10*	Figure 1A, which shows an immunoglobulin heavy chain comprising a variable region fused C-terminal to an MHC molecule . . . a chimeric protein comprising an immunoglobulin heavy chain and an MHC molecule . . . wherein the immunoglobulin heavy chain is C-terminal to the MHC molecule *page 21, claim 10*
the chimeric protein associates to form molecular complexes comprising at least two chimeric proteins per complex	the chimeric protein associates to form molecular complexes comprising at least two chimeric proteins per complex *page 4, lines 2-3*	the chimeric protein associates to form molecular complexes comprising at least two chimeric proteins per complex *page 4, lines 18-20*

an identical antigenic peptide is bound to each MHC molecule within the molecular complex	an antigenic peptide is bound to each MHC molecule, wherein each MHC molecule within the molecular complex is bound to an identical antigenic peptide *page 4, lines 3-5*	an antigenic peptide is bound to each MHC molecule, wherein each MHC molecule within the molecular complex is bound to an identical antigenic peptide *page 4, lines 20-21*

Claim 21 as amended does not encompass new matter and is entitled to the filing date of the '573 specification, September 11, 1997. As the entries in the table demonstrate, both the present specification and the '573 priority application explicitly disclose the recited composition. One skilled in the art would readily perceive that the subject matter of claim 21 as currently amended is disclosed in both specifications. Please withdraw the rejection.

Rejections Under 35 U.S.C. § 103(a)

The Final Office Action maintains two rejections under 35 U.S.C. § 103(a); each rejection cites WO 98/03552 as the primary reference:

- claims 21-23 and 53 are rejected over WO 98/03552 in view of Celluzzi,[1] Liu,[2] and Bendig;[3] and
- claims 21-23 and 53-56 are rejected over WO 98/03552 in view of Celluzzi, Liu, and Utz.[4]

Applicants respectfully traverse the rejections.

[1] Celluzzi *et al.*, *J. Exp. Med. 183*, 283-87, 1996.

[2] Liu *et al.*, *J. Exp. Med. 185*, 165-70, January 6, 1997.

[3] Bendig, Methods: A Companion to Methods in Enzymology, vol. 8, pages 83-93, 1995.

[4] Utz *et al.*, *J. Virol. 70*, 843-51, 1996.

None of the rejected claims is obvious over either of the cited combinations of references. As explained above, the claimed invention is entitled to a priority date of September 11, 1997 based on its disclosure in Serial No. 60/058,573. WO 98/03552 is not prior art to the present application because its effective date as a reference is its publication date, January 29, 1998.[5] This alone moots both rejections based on WO 98/03552.

Even if, *arguendo*, the present application were not entitled to its priority date of September 11, 1997, the rejected claims are not *prima facie* case obvious over the cited combinations of references. A *prima facie* case requires three elements:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Manual of Patent Examining Procedure, 8th ed., § 2142. The cited combinations do not disclose all the limitations of the pending claims and therefore do not render the claimed subject matter *prima facie* obvious.

The present claims are directed to a composition comprising a cell in which a chimeric protein has been bound to its surface. The chimeric protein comprises an MHC molecule and an immunoglobulin heavy chain; the immunoglobulin heavy chain comprises a variable region which is C-terminal to the MHC molecule. Two chimeric proteins associate to form a molecular complex. An identical antigenic peptide is bound to each MHC molecule within the molecular complex. Neither combination of the cited references teaches or suggests this subject matter.

[5] WO 98/03552 was filed July 15, 1997. This filing date is too early for WO 98/03552 to be cited under 35 U.S.C. § 102(e). Section 102(e) of 35 U.S.C. applies to published PCT applications filed on or after November 29, 2000. Thus, the effective date of WO 98/03552 as a reference is its publication date, January 29, 1998.

WO 98/03552 is cited as teaching "multivalent MHC complex/peptide/IgG fusion proteins." Final Office Action at page 3. But WO 98/03552 does not teach or suggest a chimeric protein or molecular complex with the features recited in claims 21-23 and 53-56. The pending claims recite a chimeric protein which comprises, *inter alia*, an immunoglobulin heavy chain comprising a variable region which is C-terminal to the MHC molecule. WO 98/03552 does not teach or suggest this feature. In fact, WO 98/03552 explicitly excludes the variable region of the immunoglobulin heavy chain: "[w]hen an immunoglobulin gene can be cleaved at the hinge region and [sic] only the gene encoding the hinge, CH2 and CH3 domains of the heavy chain is used to form the fusion protein." WO 98/03552 at page 3 ¶ 2. See also Figures 1 and 2, which teach using the constant regions of an immunoglobulin chain as a linker, but not the variable region. WO 98/03552 therefore teaches away from including the immunoglobulin heavy chain variable region at all, much less in the position recited in the pending claims.

The secondary references do not remedy the deficiencies of WO 98/03552. Celluzzi is cited as teaching the basic biology of antigen presenting cells and their function in presenting antigen to prime cytotoxic T lymphocyte (CTL) responses. Liu is cited as teaching an IgG1 isotype monoclonal antibody. Bendig is cited as teaching humanization of rodent antibodies. Utz is cited as teaching that most HLA-A2 positive individuals with HTLV-1 associated HAM-TSP have CTLs which recognize the HTLV-1 tax 11-19 peptide. None of the secondary references teaches or suggests modifying the disclosure of WO 98/03552 in a manner which would produce a chimeric protein or molecular complex with the features recited in claims 21-23 and 53-56.

The cited references must be considered in their entireties, including portions that would have led the ordinary artisan away from the claimed invention. *W.L. Gore & Associates, Inc. v.*

Garlock, Inc., 721 F.2d 1540, 1550, 220 U.S.P.Q. 303, 310 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). WO 98/03552 teaches exclusion of the heavy chain variable region. Even if WO 98/03552 were prior art to the present application (which it is not), there would be no *prima facie* case that any of claims 21-23 and 53-56 is obvious. Applicants respectfully request withdrawal of the rejection.

Respectfully submitted,

/Lisa M. Hemmendinger/

Date: April 9, 2007 By: _____

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